# FIG. 1

```
LOCUS       HSTGFB3M     2574 bp    RNA             PRI       12-SEP-1993
DEFINITION  Human mRNA for transforming growth factor-beta 3 (TGF-beta
            3).
ACCESSION   X14149
NID         g37095
KEYWORDS    growth factor; transforming growth factor; transforming
            growth factor-beta 3.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae;
            Homo.
REFERENCE   1 (bases 1 to 2574)
  AUTHORS   Chen,E.Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-MAR-1989) Chen E.Y., Genentech Inc., 460 Pt.
            San Bruno Blvd., San Francisco, CA 94080, USA
REFERENCE   2  (bases 1 to 2574)
  AUTHORS   Derynck,R., Lindquist,P.B., Lee,A., Wen,D., Tamm,J.,
            Graycar,J.L., Rhee,L., Mason,A.J., Miller,D.A.,
            Coffey,R.J., Moses,H.L. and Chen,E.Y.
  TITLE     A new type of transforming growth factor-beta, TGF-beta 3
  JOURNAL   EMBO J. 7 (12), 3737-3743 (1988)
  MEDLINE   89091120
COMMENT     See <J03241> for alternative sequence of TGF-beta 3.
FEATURES            Location/Qualifiers
     source         1..2574
                    /organism="Homo sapiens"
                    /db_xref="taxon:9606"
                    /tissue_type="placenta, ovary glioblastoma"
                    /cell_line="A172 glioblastoma"
                    /chromosome="14q24"
     CDS            254..1492
                    /note="TGF-beta 3 (AA 1-412)"
                    /codon_start=1
                    /db_xref="PID:g37096"
                    /db_xref="SWISS-PROT:P10600"
                    /translation="MKMHLQRALVVLALLNFATVSLSLSTCTTLDFGHIKKKRVEAIR
                    GQILSKLRLTSPPEPTVMTHVPYQVLALYNSTRELLEEMHGEREEGCTQENTESEYYA
                    KEIHKFDMIQGLAEHNELAVCPKGITSKVFRFNVSSVEKNRTNLFRAEFRVLRVPNPS
                    SKRNEQRIELFQILRPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTVREWLLRRESN
                    LGLEISIHCPCHTFQPNGDILENIHEVMEIKFKGVDNEDDHGRGDLGRLKKQKDHHNP
                    HLILMMIPPHRLDNPGQGGQRKKRALDTNYCFRNLEENCCVRPLYIDFRQDLGWKWVH
                    EPKGYYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASPCCVPQDLEPLTILYYV
                    GRTPKVEQLSNMVVKSCKCS"
BASE COUNT      629 a    680 c    666 g    599 t
```

# FIG. 1 (cont'd)

```
ORIGIN
    1 cctgtttaga cacatggaca acaatcccag cgctacaagg cacacagtcc gcttcttcgt
   61 cctcagggtt gccagcgctt cctggaagtc ctgaagctct cgcagtgcag tgagttcatg
  121 caccttcttg ccaagcctca gtctttggga tctggggagg ccgcctggtt ttcctccctc
  181 cttctgcacg tctgctgggg tctcttcctc tccaggcctt gccgtccccc tggcctctct
  241 tcccagctca cacatgaaga tgcacttgca aagggctctg gtggtcctgg ccctgctgaa
  301 ctttgccacg gtcagcctct ctctgtccac ttgcaccacc ttggacttcg gccacatcaa
  361 gaagaagagg gtggaagcca ttaggggaca gatcttgagc aagctcaggc tcaccagccc
  421 ccctgagcca acggtgatga cccacgtccc ctatcaggtc ctggcccttt acaacagcac
  481 ccgggagctg ctggaggaga tgcatgggga gagggaggaa ggctgcaccc aggaaaacac
  541 cgagtcggaa tactatgcca aagaaatcca taaattcgac atgatccagg ggctggcgga
  601 gcacaacgaa ctggctgtct gccctaaagg aattacctcc aaggttttcc gcttcaatgt
  661 gtcctcagtg gagaaaaata gaaccaacct attccgagca gaattccggg tcttgcgggt
  721 gcccaacccc agctctaagc ggaatgagca gaggatcgag ctcttccaga tccttcggcc
  781 agatgagcac attgccaaac agcgctatat cggtggcaag aatctgccca cacggggcac
  841 tgccgagtgg ctgtcctttg atgtcactga cactgtgcgt gagtggctgt tgagaagaga
  901 gtccaactta ggtctagaaa tcagcattca ctgtccatgt cacacctttc agcccaatgg
  961 agatatcctg gaaaacattc acgaggtgat ggaaatcaaa ttcaaaggcg tggacaatga
 1021 ggatgaccat ggccgtggag atctggggcg cctcaagaag cagaaggatc accacaaccc
 1081 tcatctaatc ctcatgatga ttcccccaca ccggctcgac aacccgggcc agggggtca
 1141 gaggaagaag cgggctttgg acaccaatta ctgcttccgc aacttggagg agaactgctg
 1201 tgtgcgcccc ctctacattg acttccgaca ggatctgggc tggaagtggg tccatgaacc
 1261 taagggctac tatgccaact tctgctcagg cccttgccca tacctccgca gtgcagacac
 1321 aacccacagc acggtgctgg gactgtacaa cactctgaac cctgaagcat ctgcctcgcc
 1381 ttgctgcgtg ccccaggacc tggagccccct gaccatcctg tactatgttg ggaggacccc
 1441 caaagtggag cagctctcca acatggtggt gaagtcttgt aaatgtagct gagaccccac
 1501 gtgcgacaga gagaggggag agagaaccac cactgcctga ctgcccgctc ctcgggaaac
 1561 acacaagcaa caaacctcac tgagaggcct ggagcccaca accttcggct ccgggcaaat
 1621 ggctgagatg gaggtttcct tttggaacat ttctttcttg ctggctctga gaatcacggt
 1681 ggtaaagaaa gtgtgggttt ggttagagga aggctgaact cttcagaaca cacagacttt
 1741 ctgtgacgca gacagagggg atggggatag aggaaaggga tggtaagttg agatgttgtg
 1801 tggcaatggg atttgggcta ccctaaaggg agaaggaagg gcagagaatg gctgggtcag
 1861 ggccagactg gaagacactt cagatctgag gttggatttg ctcattgctg taccacatct
 1921 gctctaggga atctggatta tgttatacaa ggcaagcatt ttttttttta aagacaggtt
 1981 acgaagacaa agtcccagaa ttgtatctca tactgtctgg gattaagggc aaatctatta
 2041 cttttgcaaa ctgtcctcta catcaattaa catcgtgggt cactacaggg agaaaatcca
 2101 ggtcatgcag ttcctggccc atcaactgta ttgggccttt tggatatgct gaacgcagaa
 2161 gaaagggtgg aaatcaaccc tctcctgtct gccctctggg tccctcctct cacctctccc
 2221 tcgatcatat ttccccttgg acacttggtt agacgccttc caggtcagga tgcacatttc
 2281 tggattgtgg ttccatgcag ccttggggca ttatgggtct tcccccactt cccctccaag
 2341 accctgtgtt catttggtgt tcctggaagc aggtgctaca acatgtgagg cattcgggga
 2401 agctgcacat gtgccacaca gtgacttggc cccagacgca tagactgagg tataaagaca
 2461 agtatgaata ttactctcaa aatctttgta taaataaata tttttggggc atcctggatg
 2521 atttcatctt ctggaatatt gtttctagaa cagtaaaagc cttattctaa ggtg
//
```

# FIG. 2

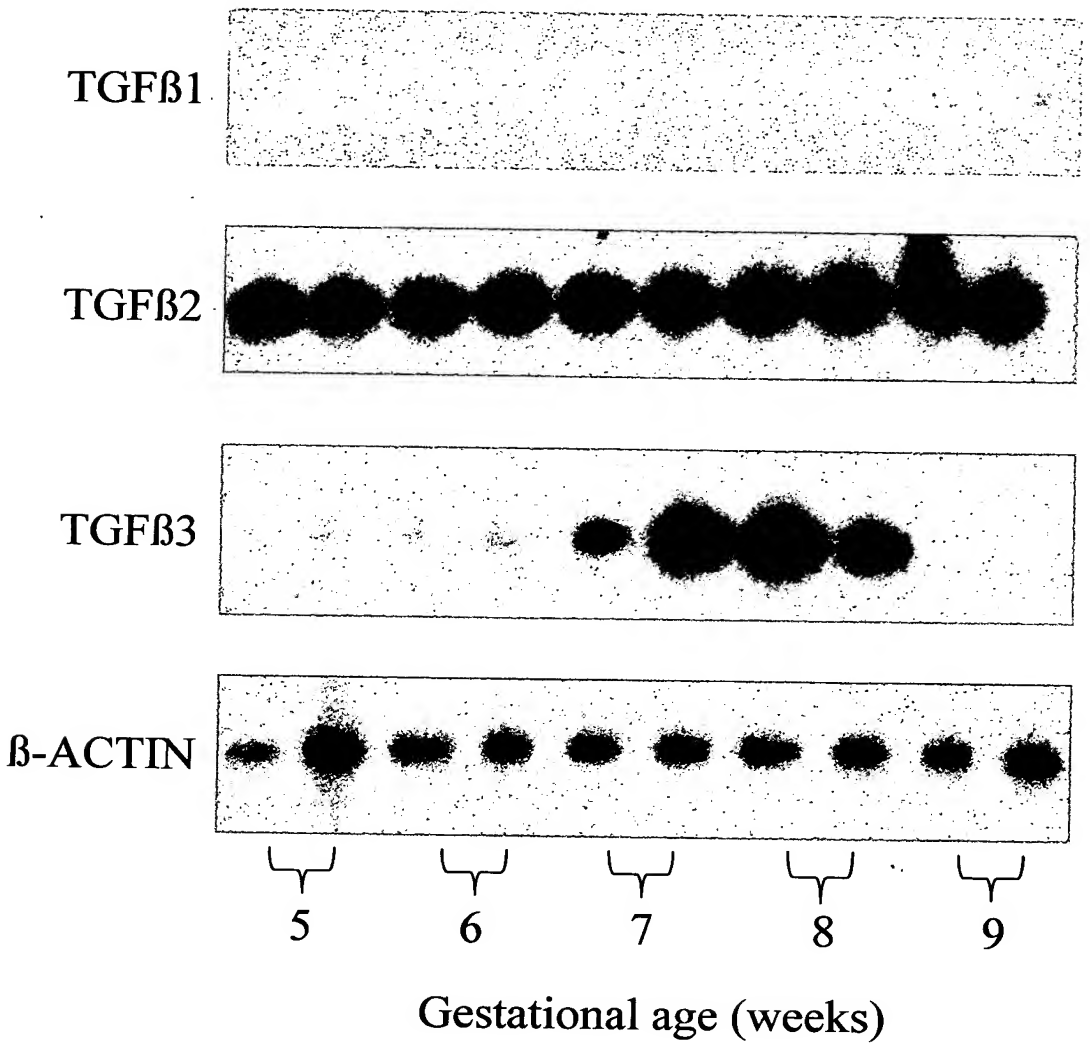
```
LOCUS       HSU22431     3678 bp    mRNA            PRI       28-JUN-1995
DEFINITION  Human hypoxia-inducible factor 1 alpha (HIF-1 alpha) mRNA, complete
            cds.
ACCESSION   U22431
NID         g881345
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3678)
  AUTHORS   Wang,G.L., Jiang,B.H., Rue,E.A. and Semenza,G.L.
  TITLE     Hypoxia-inducible factor 1 is a basic-helix-loop-helix-PAS
            heterodimer regulated by cellular O2 tension
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 92 (12), 5510-5514 (1995)
  MEDLINE   95296340
REFERENCE   2  (bases 1 to 3678)
  AUTHORS   Wang,G.L., Jiang,B.-H., Rue,E.A. and Semenza,G.L.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-MAR-1995) Gregg L. Semenza, Center for Medical
            Genetics, The Johns Hopkins University School of Medicine, 600 N.
            Wolfe St., Baltimore, MD 21287-3914, USA
FEATURES             Location/Qualifiers
     source          1..3678
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /cell_line="Hep3B"
                     /cell_type="hepatoblastoma"
     gene            29..2509
                     /gene="HIF-1 alpha"
     CDS             29..2509
                     /gene="HIF-1 alpha"
                     /standard_name="hypoxia-inducible factor 1, alpha subunit"
                     /note="basic helix-loop-helix transcription factor"
                     /codon_start=1
                     /product="hypoxia-inducible factor 1 alpha"
                     /db_xref="PID:g881346"
                     /translation="MEGAGGANDKKKISSERRKEKSRDAARSRRSKESEVFYELAHQL
                     PLPHNVSSHLDKASVMRLTISYLRVRKLLDAGDLDIEDDMKAQMNCFYLKALDGFVMV
                     LTDDGDMIYISDNVNKYMGLTQFELTGHSVFDFTHPCDHEEMREMLTHRNGLVKKGKE
                     QNTQRSFFLRMKCTLTSRGRTMNIKSATWKVLHCTGHIHVYDTNSNQPQCGYKKPPMT
                     CLVLICEPIPHPSNIEIPLDSKTFLSRHSLDMKFSYCDERITELMGYEPEELLGRSIY
                     EYYHALDSDHLTKTHHDMFTKGQVTTGQYRMLAKRGGYVWVETQATVIYNTKNSQPQC
                     IVCVNYVVSGIIQHDLIFSLQQTECVLKPVESSDMKMTQLFTKVESEDTSSLFDKLKK
                     EPDALTLLAPAAGDTIISLDFGSNDTETDDQQLEEVPLYNDVMLPSPNEKLQNINLAM
                     SPLPTAETPKPLRSSADPALNQEVALKLEPNPESLELSFTMPQIQDQTPSPSDGSTRQ
                     SSPEPNSPSEYCFYVDSDMVNEFKLELVEKLFAEDTEAKNPFSTQDTDLDLEMLAPYI
                     PMDDDFQLRSFDQLSPLESSSASPESASPQSTVTVFQQTQIQEPTANATTTTATTDEL
                     KTVTKDRMEDIKILIASPSPTHIHKETTSATSSPYRDTQSRTASPNRAGKGVIEQTEK
                     SHPRSPNVLSVALSQRTTVPEEELNPKILALQNAQRKRKMEHDGSLFQAVGIGTLLQQ
                     PDDHAATTSLSWKRVKGCKSSEQNGMEQKTIILIPSDLACRLLGQSMDESGLPQLTSY
                     DCEVNAPIQGSRNLLQGEELLRALDQVN"
     polyA_site      3678
                     /note="42 A nucleotides"
BASE COUNT     1197 a    695 c    675 g   1111 t
```

# FIG. 2 (cont'd)

ORIGIN

```
       1 gtgaagacat cgcggggacc gattcaccat ggagggcgcc ggcggcgcga acgacaagaa
      61 aaagataagt tctgaacgtc gaaaagaaaa gtctcgagat gcagccagat ctcggcgaag
     121 taaagaatct gaagtttttt atgagcttgc tcatcagttg ccacttccac ataatgtgag
     181 ttcgcatctt gataaggcct ctgtgatgag gcttaccatc agctatttgc gtgtgaggaa
     241 acttctggat gctggtgatt tggatattga agatgacatg aaagcacaga tgaattgctt
     301 ttatttgaaa gccttggatg gttttgttat ggttctcaca gatgatggtg acatgattta
     361 catttctgat aatgtgaaca aatacatggg attaactcag tttgaactaa ctggacacag
     421 tgtgtttgat tttactcatc catgtgacca tgaggaaatg agagaaatgc ttacacacag
     481 aaatggcctt gtgaaaaagg gtaaagaaca aaacacacag cgaagctttt ttctcagaat
     541 gaagtgtacc ctaactagcc gaggaagaac tatgaacata aagtctgcaa catggaaggt
     601 attgcactgc acaggccaca ttcacgtata tgataccaac agtaaccaac ctcagtgtgg
     661 gtataagaaa ccacctatga cctgcttggt gctgatttgt gaacccattc ctcacccatc
     721 aaatattgaa attcctttag atagcaagac tttcctcagt cgacacagcc tggatatgaa
     781 attttcttat tgtgatgaaa gaattaccga attgatggga tatgagccag aagaactttt
     841 aggccgctca atttatgaat attatcatgc tttggactct gatcatctga ccaaaactca
     901 tcatgatatg tttactaaag gacaagtcac cacaggacag tacaggatgc ttgccaaaag
     961 aggtggatat gtctgggttg aaactcaagc aactgtcata tataacacca agaattctca
    1021 accacagtgc attgtatgtg tgaattacgt tgtgagtggt attattcagc acgacttgat
    1081 tttctccctt caacaaacag aatgtgtcct taaaccggtt gaatcttcag atatgaaaat
    1141 gactcagcta ttcaccaaag ttgaatcaga agatacaagt agcctctttg acaaacttaa
    1201 gaaggaacct gatgctttaa ctttgctggc cccagccgct ggagacacaa tcatatcttt
    1261 agattttggc agcaacgaca cagaaactga tgaccagcaa cttgaggaag taccattata
    1321 taatgatgta atgctccccc cacccaacga aaaattacag aatataaatt tggcaatgtc
    1381 tccattaccc accgctgaaa cgccaaagcc acttcgaagt agtgctgacc ctgcactcaa
    1441 tcaagaagtt gcattaaaat tagaaccaaa tccagagtca ctggaacttt cttttaccat
    1501 gccccagatt caggatcaga cacctagtcc ttccgatgga agcactagac aaagttcacc
    1561 tgagcctaat agtcccagtg aatattgttt ttatgtggat agtgatatgg tcaatgaatt
    1621 caagttggaa ttggtagaaa aacttttgc tgaagacaca gaagcaaaga acccatttc
    1681 tactcaggac acagatttag acttggagat gttagctccc tatatcccaa tggatgatga
    1741 cttccagtta cgttccttcg atcagttgtc accattagaa agcagttccg caagccctga
    1801 aagcgcaagt cctcaaagca cagttacagt attccagcag actcaaatac aagaacctac
    1861 tgctaatgcc accactacca ctgccaccac tgatgaatta aaaacagtga caaaagaccg
    1921 tatggaagac attaaaatat tgattgcatc tccatctcct acccacatac ataaagaaac
    1981 tactagtgcc acatcatcac catatagaga tactcaaagt cggacagcct caccaaacag
    2041 agcaggaaaa ggagtcatag aacagacaga aaaatctcat ccaagaagcc ctaacgtgtt
    2101 atctgtcgct ttgagtcaaa gaactacagt tcctgaggaa gaactaaatc caaagatact
    2161 agctttgcag aatgctcaga gaaagcgaaa aatggaacat gatggttcac tttttcaagc
    2221 agtaggaatt ggaacattat tacagcagcc agacgatcat gcagctacta catcactttc
    2281 ttggaaacgt gtaaaaggat gcaaatctag tgaacagaat ggaatggagc aaaagacaat
    2341 tattttaata ccctctgatt tagcatgtag actgctgggg caatcaatgg atgaaagtgg
    2401 attaccacag ctgaccagtt atgattgtga agttaatgct cctatacaag gcagcagaaa
    2461 cctactgcag ggtgaagaat tactcagagc tttggatcaa gttaactgag ctttttctta
    2521 atttcattcc tttttttgga cactggtggc tcactaccta aagcagtcta tttatatttt
    2581 ctacatctaa ttttagaagc ctggctacaa tactgcacaa acttggttag ttcaattttt
    2641 gatccccttt ctacttaatt tacattaatg ctctttttta gtatgttctt taatgctgga
    2701 tcacagacag ctcatttttct cagtttttg gtatttaaac cattgcattg cagtagcatc
    2761 attttaaaaa atgcaccttt ttatttattt atttttggct agggagttta tccctttttc
    2821 gaattatttt taagaagatg ccaatataat ttttgtaaga aggcagtaac ctttcatcat
    2881 gatcataggc agttgaaaaa tttttacacc tttttttca catttacat aaataataat
    2941 gctttgccag cagtacgtgg tagccacaat tgcacaatat attttcttaa aaaataccag
    3001 cagttactca tggaatatat tctgcgttta taaaactagt ttttaagaag aaatttttt
    3061 tggcctatga aattgttaaa cctggaacat gacattgtta atcatataat aatgattctt
    3121 aaatgctgta tggtttatta tttaaatggg taaagccatt tacataatat agaaagatat
    3181 gcatatatct agaaggtatg tggcatttat ttggataaaa ttctcaattc agagaaatca
    3241 tctgatgttt ctatagtcac tttgccagct caaaagaaaa caatacccta tgtagttgtg
    3301 gaagtttatg ctaatattgt gtaactgata ttaaacctaa atgttctgcc taccctgttg
    3361 gtataaagat attttgagca gactgtaaac aagaaaaaaa aaatcatgca ttcttagcaa
    3421 aattgcctag tatgttaatt tgctcaaaat acaatgtttg attttatgca ctttgtcgct
    3481 attaacatcc tttttttcat gtagatttca ataattgagt aattttagaa gcattatttt
    3541 aggaatatat agttgtcaca gtaaatatct tgtttttttct atgtacattg tacaaatttt
    3601 tcattccttt tgctctttgt ggttggatct aacactaact gtattgtttt gttacatcaa
    3661 ataaacatct tctgtgga
```

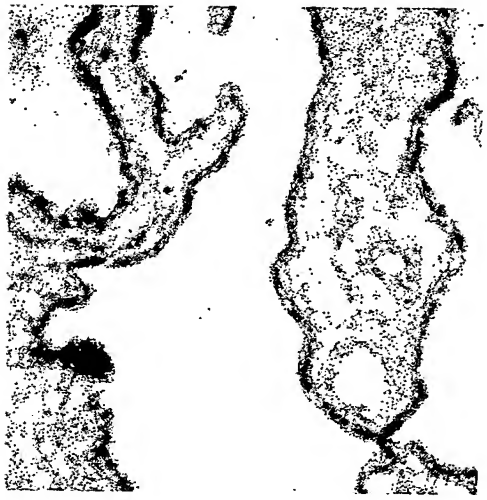
FIG. 3A



# FIG. 3B

5 weeks


8 weeks



12 weeks

8 weeks (control)

# FIG. 4A

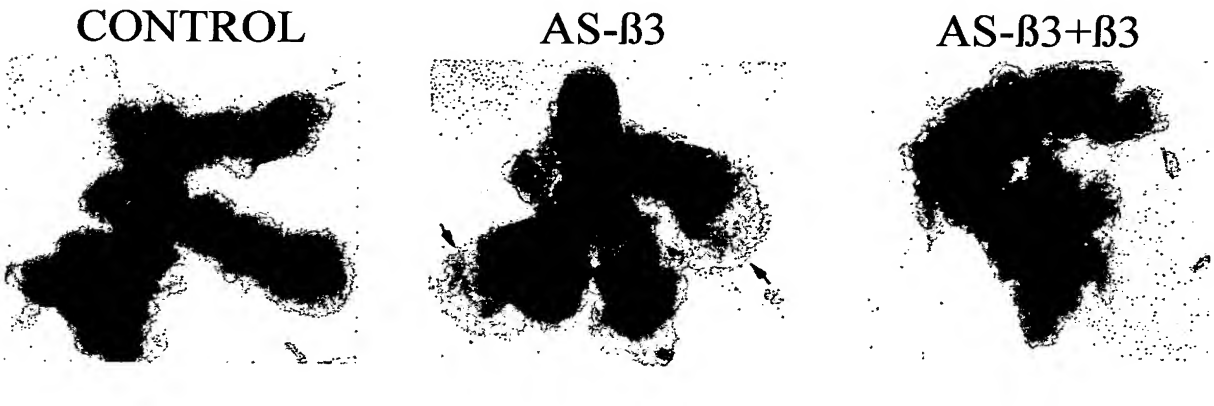


FIG. 4B

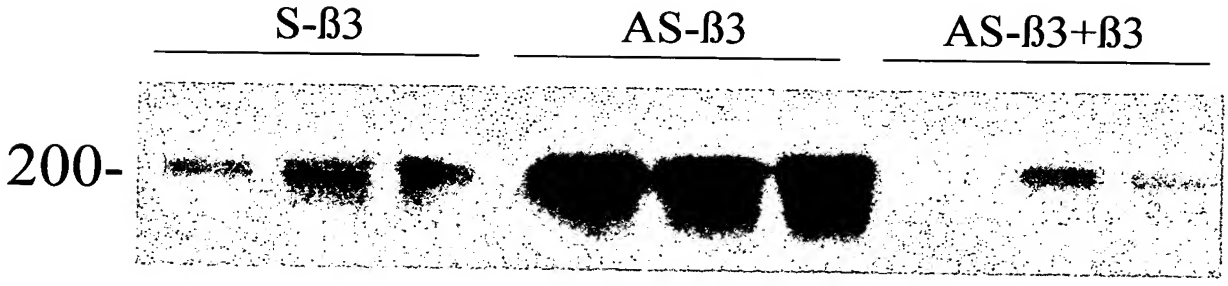


FIG. 4C

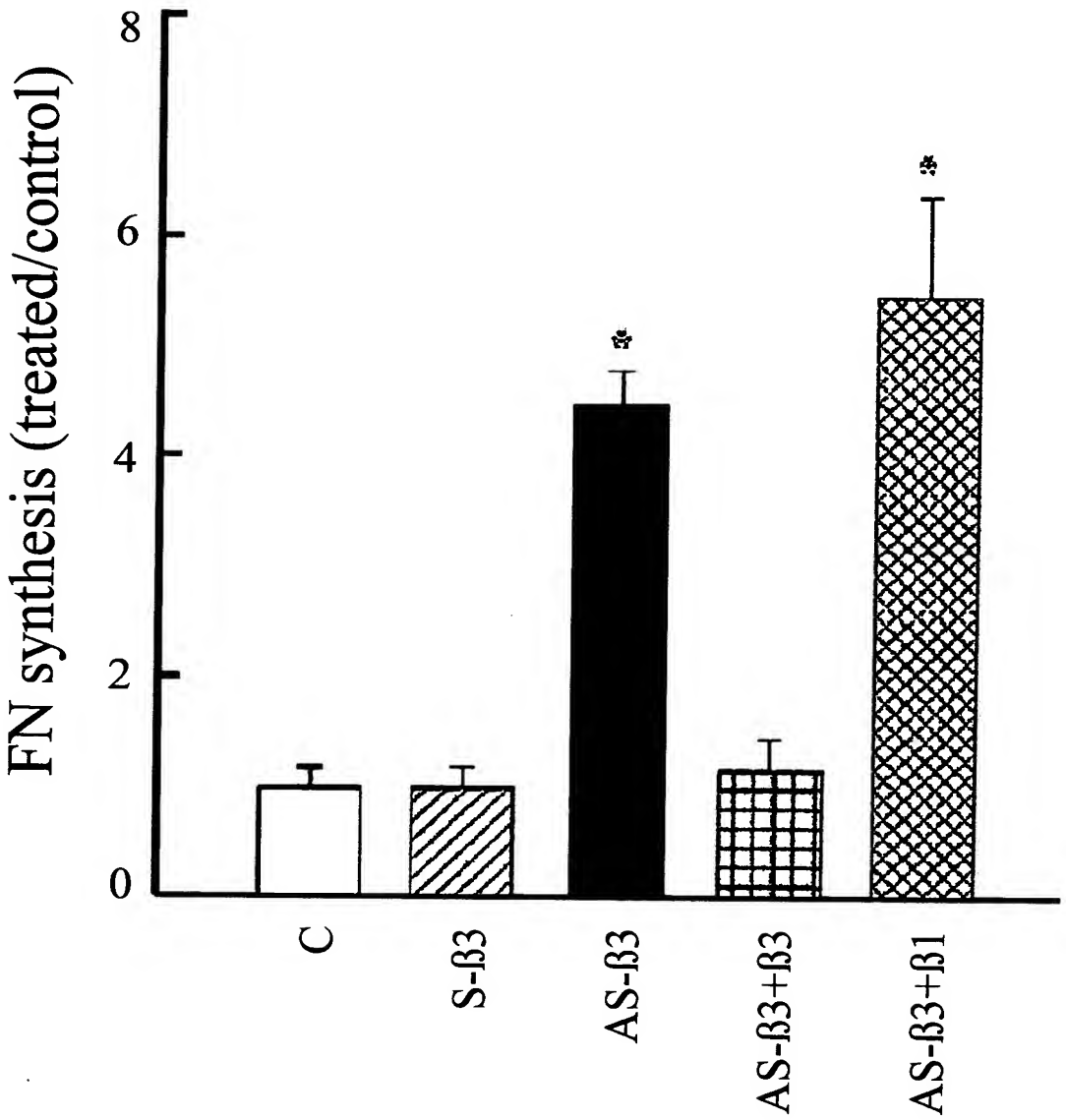

FN synthesis (treated/control)
8
6
4
2
0
C
S-ß3
AS-ß3
AS-ß3+ß3
AS-ß3+ß1

FIG. 4D

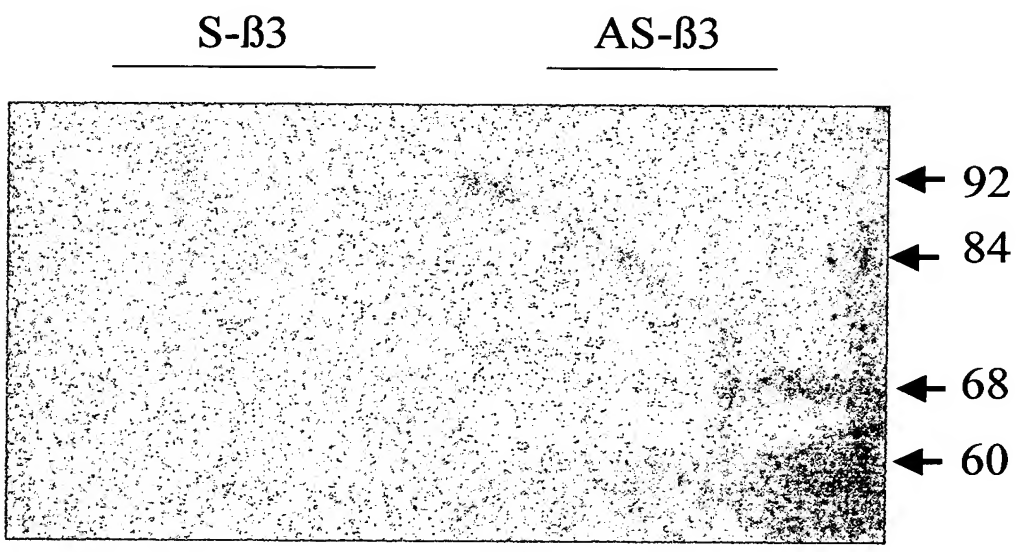


FIG. 4E

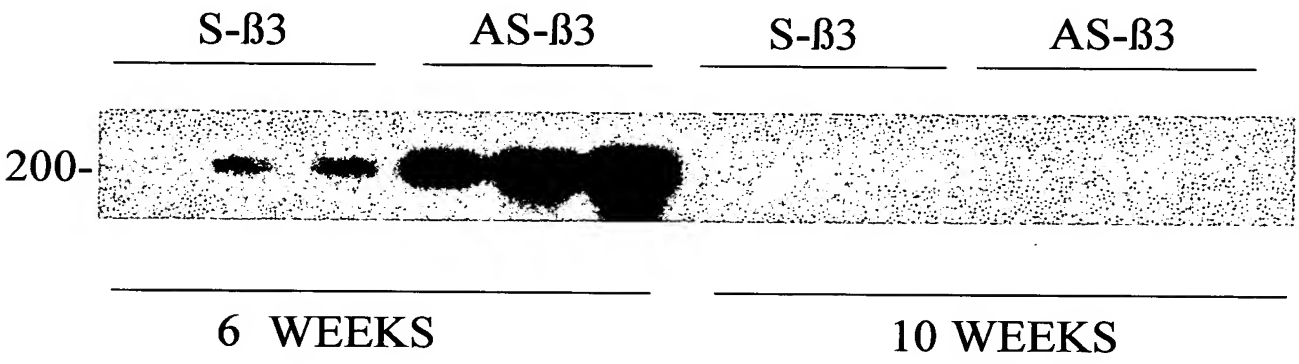
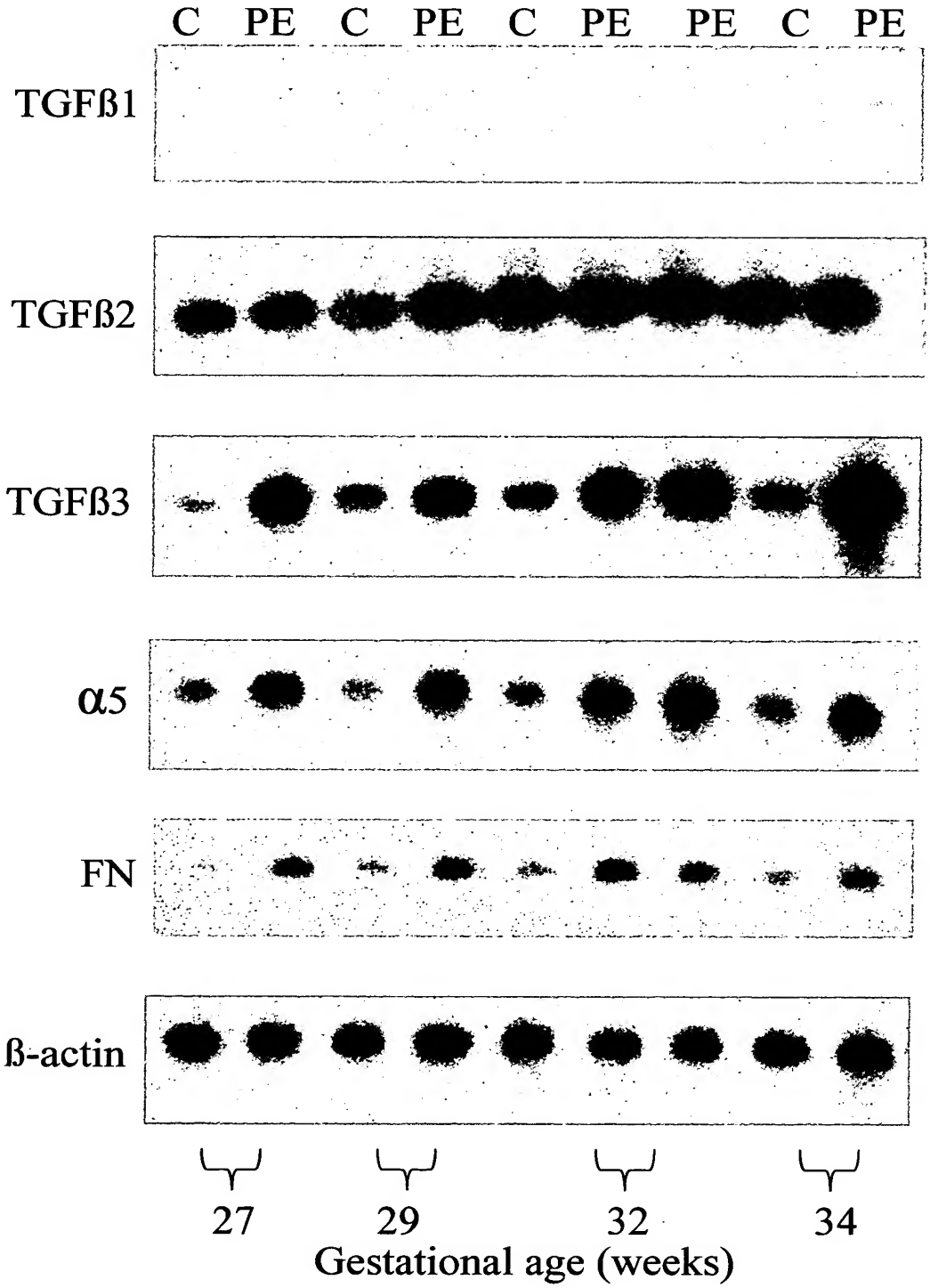
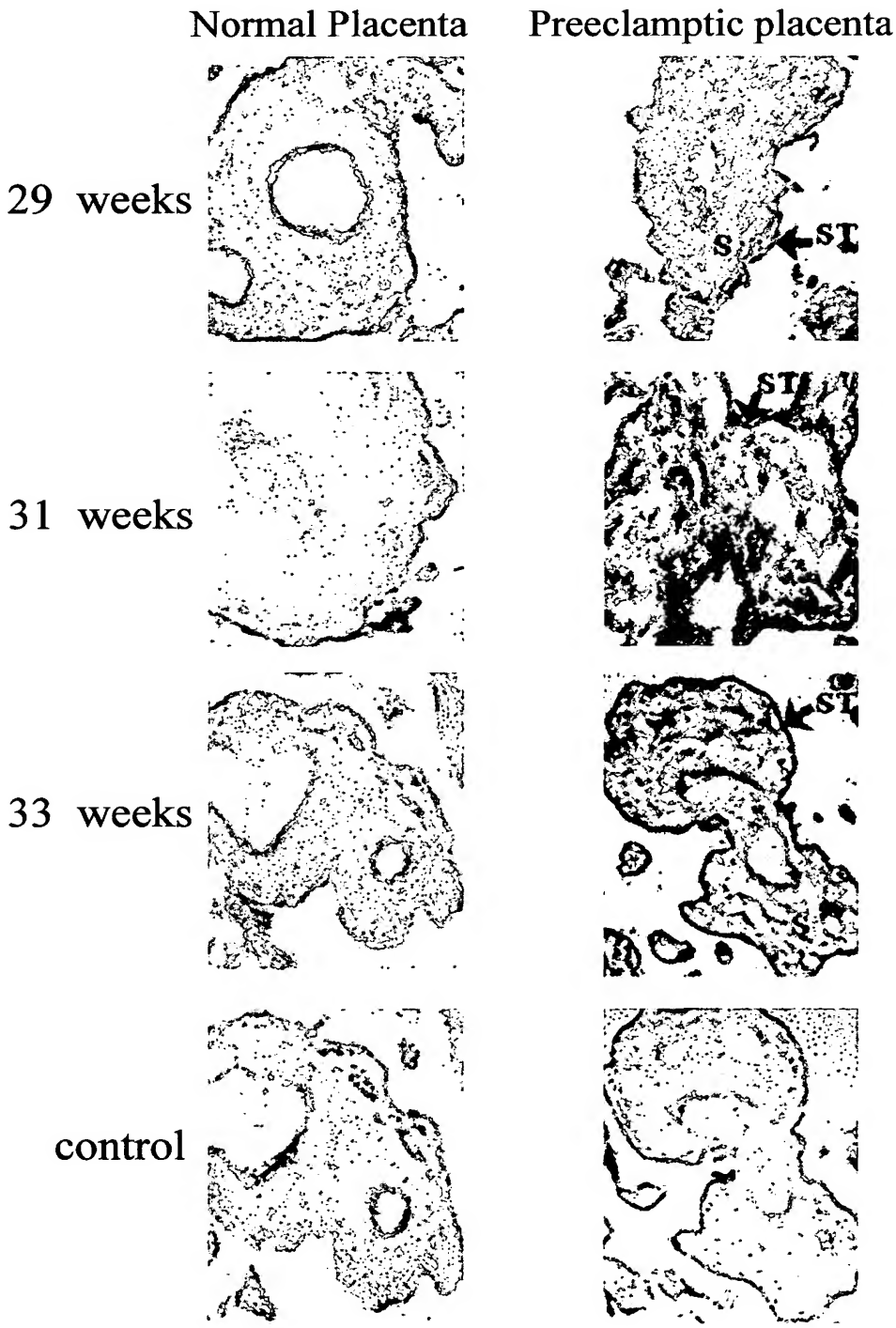


FIG. 5A


C PE C PE C PE PE C PE
TGFß1
TGFß2
TGFß3
α5
FN
ß-actin
27
29
32
34
Gestational age (weeks)

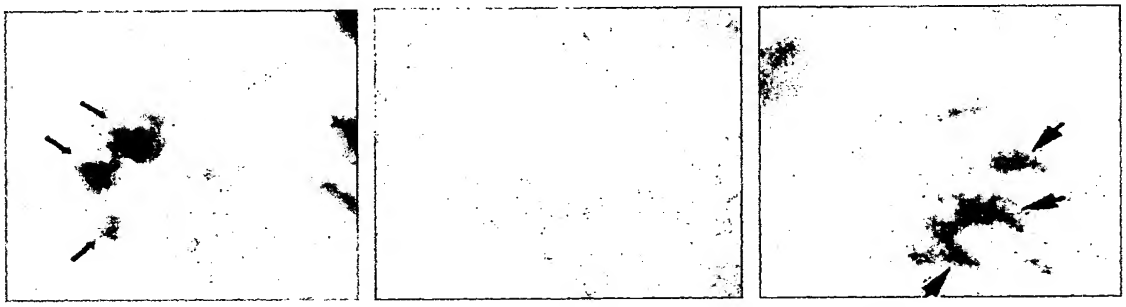
# FIG. 5B


Normal Placenta
Preeclamptic placenta
29 weeks
31 weeks
33 weeks
control
S
ST
ST
ST

# FIG. 6A

Normal Placenta

Preeclamptic placenta



S-ß3

S-ß3

AS-ß3

# FIG. 6B

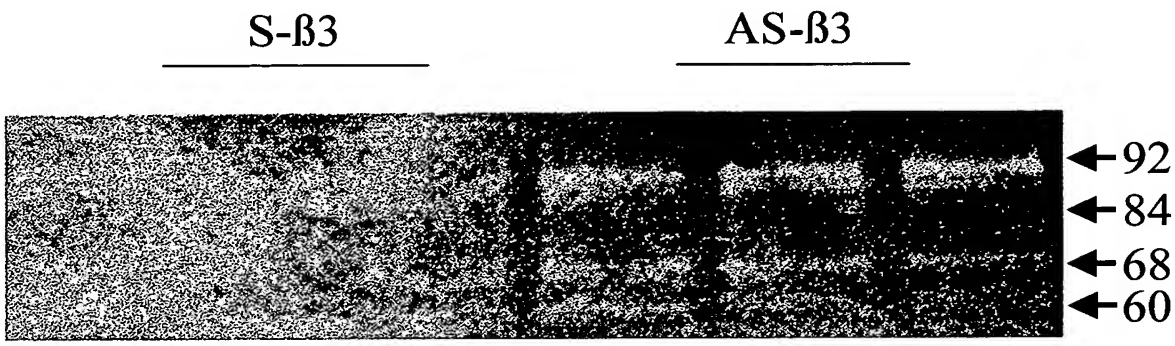


FIG. 6C

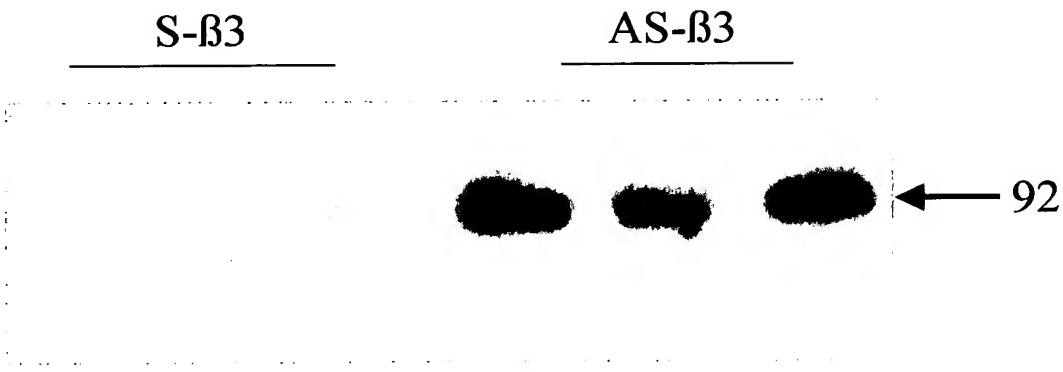


FIG. 7A

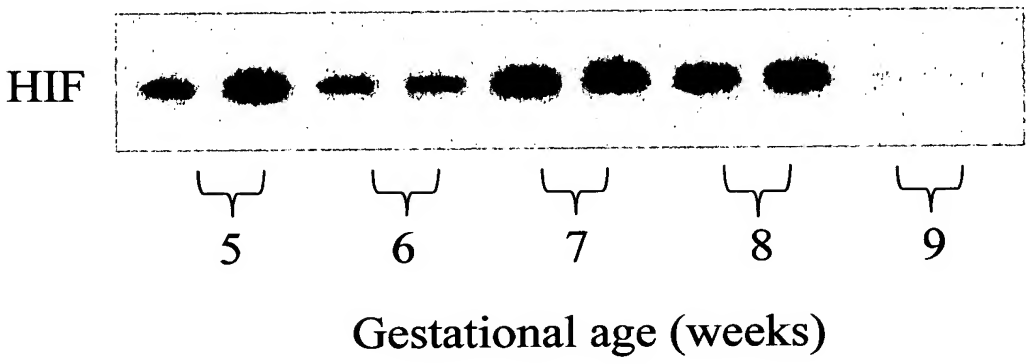
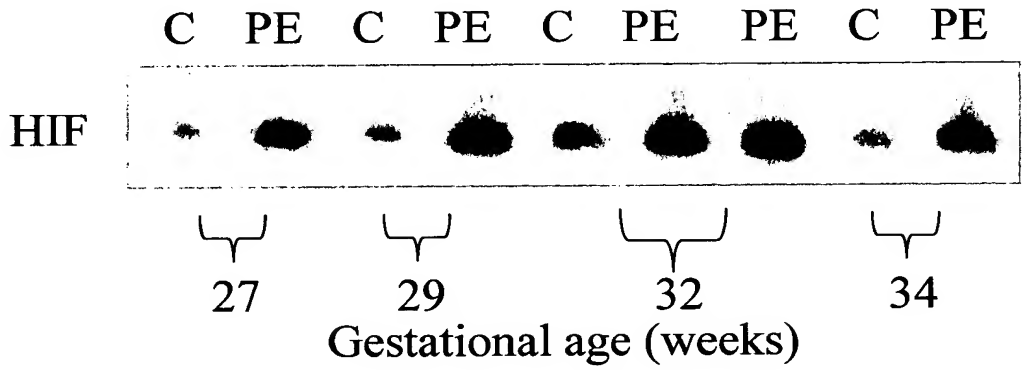
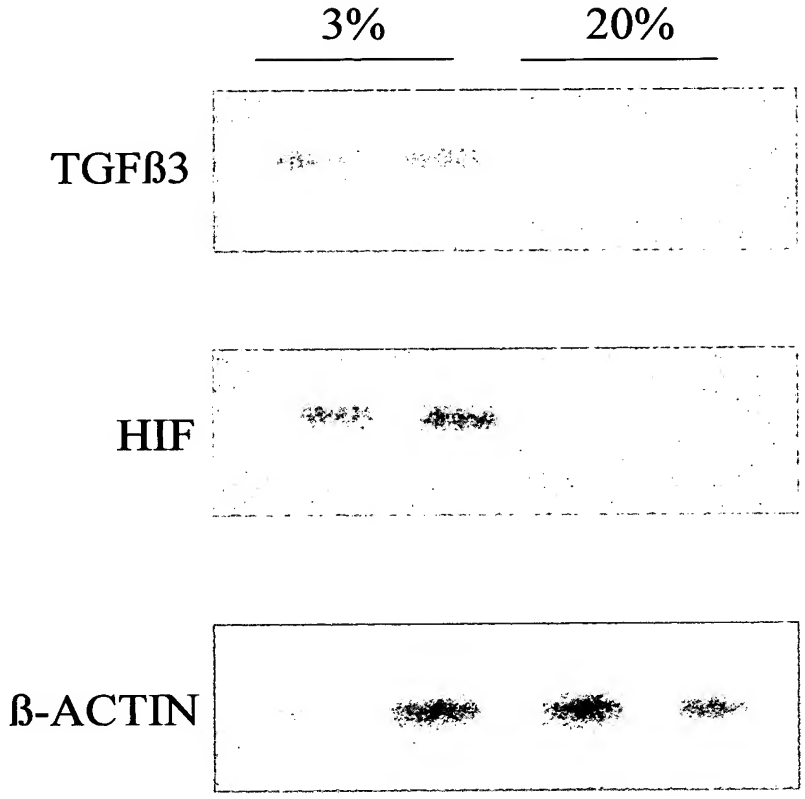


FIG. 7B



# FIG. 8



# FIG. 9

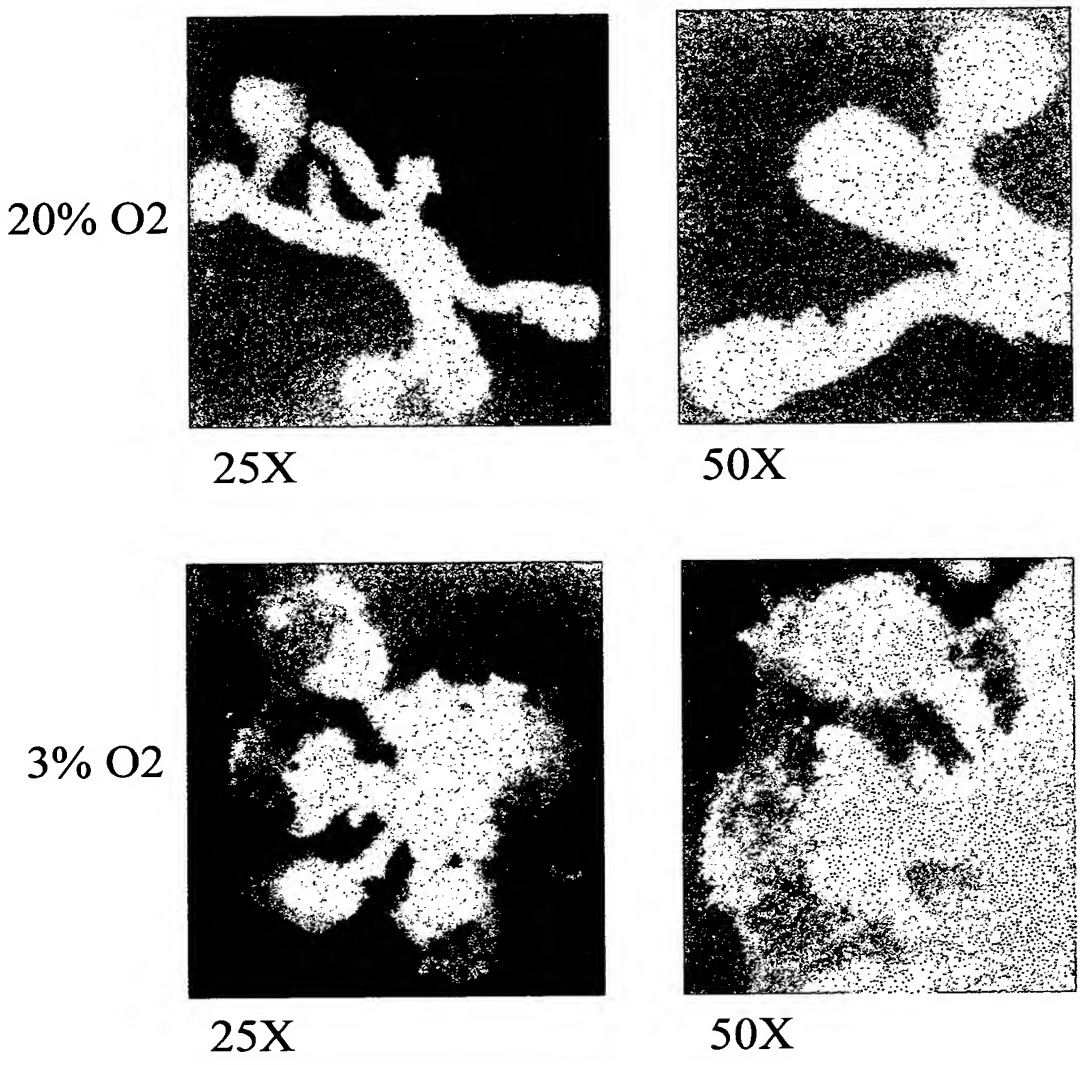


FIG. 10